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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,557	06/04/2007	Maher Kalaji	31229-232367	4750

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EXAMINER	
DINH, BACH T	

ART UNIT	PAPER NUMBER
1724	

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12/20/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,557	KALAJI ET AL.	
	Examiner	Art Unit	
	BACH DINH	1724	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-28* is/are pending in the application.

5a) Of the above claim(s) *17-27* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-16 and 28* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 08/15/2011 has been entered.

Summary

2. This is the response to the communication filed on 08/15/2011.

3. Claims 1-28 are currently pending with claims 17-27 are withdrawn from consideration.

4. The application is not in condition for allowance.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 1-7, 9, 13, 16 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Ruger et al. (US 5,834,224) and Urry (US 2002/0068304) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claim 1-7 and 28, Willner discloses a sensing device (figure 1) comprising an electrode 1 comprising a noble metal layer (col. 9 lines 29-37 or 9:29-37, gold electrode), on which a layer 4 of glutathione reductase (9:46-50) is immobilized on the gold electrode (Abstract). Furthermore, Willner discloses the biological material comprises a plurality of sulphur-containing functional groups (figures 20 and 22).

Shah discloses that glutathione reductase catalyzes nitroaromatic compounds (3:18-35); therefore, the glutathione reductase is a nitroreductase enzyme.

Willner is silent regarding the biological material comprises a plurality of cysteine residues adsorb directly to the noble metal layer.

Ruger discloses an electrochemical sensor comprises enzymes (3:62-4:30) that are immobilized onto a noble metal layer (3:1-9) via a plurality of cysteine linkages (4:14-24, 6:14-19).

Urry discloses forming cysteine residues at the end of a biological molecule in order to attach the biological molecule to gold surface via the thiol -SH bond ([0084, 0127]).

At the time of the invention, one of ordinary skill in the art would have found it obvious to modify the sensing device of Willner with the plurality of cysteine residues as disclosed by Ruger and absorbing the plurality of cysteine residues directly to the gold

surface via the thiol -SH bond as disclosed by Urry because the bond between the cysteine residues of the modified enzyme to the substrate is formed at the N- or/and -C terminus, which does not impede the active center of the enzyme that is essential for enzymatic activity (Ruger, 4:43-49) and absorbing the -SH functional group of the cysteine residues to the gold surface as disclosed by Urry [0084,0127] provides the required thiol bond by Willner (figures 8, 20 and 22).

Addressing claim 9, Willner discloses the electrode comprises a semi-permeable membrane that encloses the electrode and is permeable to the analyte (5:62-65); therefore, the immobilized enzyme is also covered by the semi-permeable membrane or the fluid permeable cover layer.

Addressing claim 13, Willner discloses the noble metal layer is gold (2:63-69).
Ruger discloses the noble metal layer is gold (3:1-9).
Furthermore, the limitation of current claim is drawn to the process of forming the biological material on the noble metal layer, which does not further structurally limit the claimed sensing device (please see MPEP 2112.01). For the purpose of examination, the limitation of current is treated as a layer of nitroreductase is attached to the gold layer via a plurality of cysteine residues at a location on the enzyme that does not interfere with the activity of the enzyme.
In the modification discussed in the rejection of claim 1, the plurality of cysteine residues are used for immobilizing the enzyme onto the noble metal layer; therefore, the plurality

of cysteine residues are at a location that does not interfere with the enzymatic activity (Ruger, 4:45-49).

Addressing claim 16, Willner discloses the nitroreductase is operably associated with an electron mediator (5:47-57).

8. Claims 8 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Ruger et al. (US 5,834,224) and Urry (US 2002/0068304) as applied to claims 1-7, 9, 13, 16 and 28 above, and further in view of Grove et al. (WO 03/018788) and Shah et al. (US 5,777,190).

Addressing claim 8, it is noticed from the originally filed specification the SEQ ID1 and SEQ ID2 refer to the nfnB gene in *E. coli* and pnrA gene in *P. putida*, respectively. Furthermore, the limitation of current claim is drawn to the process of making the nitroreductase enzyme, which does not further structurally limit the claimed sensing device (please see MPEP 2112.01). For the purpose of examination, the claim is treated as nitroreductase enzyme encoded by either the nfnB gene or pnrA gene according to the originally filed specification.

Willner is silent regarding the nitroreductase enzyme is encoded by either the nfnB gene or pnrA gene.

Grove discloses nitroreductase enzyme; wherein, the nitroreductase enzyme is encoded by the nfsB gene or nfnB gene (page 2 line 16 to page 3 line 19).

Shah discloses using nitroreductase enzyme to control the reduction of nitroaromatic compounds (1:13-15).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the enzyme of Willner with the nitroreductase enzyme as disclosed by Grove because the nitroreductase enzyme of Grove, which reduces nitroaromatic compounds, would allow one to measure explosives such as TNT (Shah, 2:31-44).

Addressing claims 14-15, it is noticed from the originally filed specification that the SEQ ID3 is the nfnB gene with genetic sequence to express a 6 cysteine residues inserted at the N-terminal end (page 7 lines 23-29 of the specification) and the SEQ ID5 is the pnrA gene with genetic sequence to express a 6 cysteine residues inserted at the N-terminal end (page 7 line 31 to page 8 line 4). Furthermore, SEQ ID4 and SEQ ID6 are the nitroreductase enzymes as the translation products of SEQ ID3 and SEQ ID5, respectively (page 8 lines 6-9). In other words, SEQ ID4 is the nitroreductase enzyme expressed by the nfnB gene with a six cysteine residues attached at the N-terminal; likewise, SEQ ID6 is the nitroreductase enzyme expressed by the pnrA gene with a six cysteine residues attached at the N-terminal. Additionally, the limitation of current claim is drawn to the process of binding the nitroreductase enzyme to the gold electrode, which does not structurally limit the claimed sensing device (please see MPEP 2112.01). For the purpose of examination, the limitation of claims 14 and 15 in light of claim 13 is treated as the nitroreductase enzyme expressed by the nfnB gene or pnrA gene is attached

to the gold electrode via the six cysteine residues provided at the N-terminal of the nitroreductase enzyme.

Willner is silent regarding the nitroreductase enzyme is encoded by either the nfnB gene or pnrA gene having six cysteine residues attached at the N-terminal for binding the enzyme to the gold electrode.

Grove discloses nitroreductase enzyme; wherein, the nitroreductase enzyme is encoded by the nfsB gene or nfnB gene (page 2 line 16 to page 3 line 19).

Shah discloses using nitroreductase enzyme to control the reduction of nitroaromatic compounds (1:13-15).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the enzyme of Willner with the nitroreductase enzyme as disclosed by Grove because the nitroreductase enzyme of Grove, which reduces nitroaromatic compounds, would allow one to measure explosives such as TNT (Shah, 2:31-44).

Ruger discloses an electrochemical sensor; wherein, the enzyme is modified at the N-terminal attachment with a plurality of cysteine residues (4:13-24) at a location that does not interfere with the enzymatic activity (4:45-49) for binding the enzyme to the supporting material of gold or platinum (3:1-9).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the sensing device of Willner by modifying the nitroreductase enzyme disclosed by Grove with the plurality of cysteine residues at the N-terminal in the manner disclosed by Ruger because the plurality of cysteine residues would enhance the bond between the nitroreductase enzyme and the electrode, providing the thiol binding groups

required by Willner and provide high covering density of enzyme coupled with high conductivity and sensitivity (Ruger, 2:24-29). Additionally, it would have been obvious for one with ordinary skill in the art to modify the N-terminal of the nitroreductase enzyme of Grove with six cysteine residues because Ruger already discloses the inclusion of a plurality of cysteine residues at the N-terminal; therefore, absent of contrary support to show criticality, choosing to incorporate six cysteine residues is obvious as a matter of engineering choice and is well within the technical grasp of one with ordinary skill in the art. Furthermore, the amount of cysteine residues at the N-terminal affects the bond between the enzyme and the electrode; therefore, one would have arrived at the six cysteine residues at the N-terminal of the nitroreductase enzyme when performing routine experiment with the amount of cysteine residues incorporated at the N-terminal of the enzyme in order to optimize the bond between the enzyme and the electrode.

9. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Ruger et al. (US 5,834,224) and Urry (US 2002/0068304) as applied to claims 1-7, 9, 13, 16 and 28 above, and further in view of Matsumoto et al. (US 5,795,774) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claim 10, Willner is silent regarding the cover layer comprises a polycarbonate or polyacrylate material.

Matsumoto discloses a biosensor; wherein, polycarbonate is used as a layer for allowing the diffusion of analyte while restricting the diffusion of macromolecules (2:15-31).

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the membrane of Willner with the polycarbonate material of Matsumoto because the polycarbonate material restricts the diffusion of macromolecules while allowing the diffusion of the analyte; thereby, increasing the range of concentrations which the sensor could be used to measure (Matsumoto, 2:22-26).

10. Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (US 5,443,701) in view of Ruger et al. (US 5,834,224) and Urry (US 2002/0068304) as applied to claims 1-7, 9, 13, 16 and 28 above, and further in view of Saini et al. (US 5,521,101) with further evidence provided by Shah et al. (US 5,777,190).

Addressing claims 11-12, Willner is silent regarding the noble metal layer is mounted on an insulating substrate and is connected to a surface not comprising the biological material, to one or more layers of conductive, semi-conductive or insulating material. Saini discloses a sensor for measuring TNT like that of Willner; wherein, the gold electrodes (9:65-67) are mounted on an insulating substrate 4 (10:9, quartz substrate) or a surface not comprising the biological material.

At the time of the invention, one with ordinary skill in the art would have found it obvious to modify the device of Willner with the insulating substrate in the manner disclosed by Saini because the insulating substrate would provide support for the gold electrode (Saini, figure 1, 10:8-9).

Response to Arguments

11. The Request for Information in the previous Office Action is withdrawn in view of Applicant's affidavit.

12. Applicant's arguments with respect to claims 1-16 and 28 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BACH DINH whose telephone number is (571)270-5118. The examiner can normally be reached on Monday-Friday EST 7:00 A.M-3:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Keith Hendricks can be reached on (571)272-1401. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BD
12/16/2011

/Keith D. Hendricks/

Supervisory Patent Examiner, Art Unit 1724